

## REMARKS

Claims 72, 86, 126-159, and 168-202 are pending in the application. Claims 72, 86, 126-159, and 195-202 are canceled as being drawn to a non-elected invention without prejudice to applicants' right to pursue the canceled subject matter in one or more subsequent applications. Claims 168-194 have been examined and stand rejected. Claims 168, 178, and 188 have been amended. No new matter has been introduced. Reconsideration and allowance of Claims 168-194 is respectfully requested.

### The Rejection of Claims 168-194 Under 35 U.S.C. § 101

Claims 168-194 stand rejected under 35 U.S.C. § 101 based on non-statutory subject matter and lack of utility. The Examiner notes that each independent claim is directed to a method of identifying a molecular target and asserts that recited process steps do not recite any positive physical limitation wherein physical steps or interactions occur. The Examiner concludes that the instant claims are directed to non-statutory subject matter because they lack a tie to a particular machine or apparatus and do not involve any transformation of a particular article into a different state or thing. Applicants respectfully traverse this ground of rejection for at least the following reasons.

In order to facilitate prosecution, independent Claim 188 (from which Claims 169-177 depend) and independent Claim 178 (from which Claims 179-187 depend) have been amended to include the recitation "wherein at least one of steps (a), (b), and (c) is performed by a suitably programmed computer."

Independent Claim 188 (from which Claims 189-194 depend) has been amended to include the recitation "wherein at least one of steps (a) and (b) is performed by a suitably

programmed computer." Support for these amendments is found in the specification as filed, published as WO 2004/061616; for example, at page 27, line 18, to page 29, line 10.

Accordingly, removal of this ground of rejection is respectfully requested.

#### The Rejection of Claims 168-194 Under 35 U.S.C. § 101 as Lacking Utility

Claims 168-194 stand rejected under 35 U.S.C. § 101 as lacking utility. The Examiner asserts that the instant claims do not recite any positive limitation wherein physical steps or interactions occur. The Examiner further asserts that the instant claims do not recite any particular improvement or resultant characteristic that is imparted to genes identified by the instant method or how analysis of the resultant sequences would be used to yield any useful information. Applicants respectfully traverse this ground of rejection for at least the following reasons.

It is noted that independent Claim 168, as amended, specifies a method of identifying a molecular target for a second trait in a second species, the method comprising:

- (a) identifying a first gene in a segregating population that is causal for a first trait exhibited by all or a portion of said segregating population, wherein each member of said segregating population is a member of a first species and wherein said second trait in said second species corresponds to said first trait in said first species;
- (b) mapping said first gene in said first species to a corresponding locus in the genome of the second species; and
- (c) determining whether a marker or a haplotype in said corresponding locus in the genome of the second species associates with said second trait, wherein, when said marker or said haplotype associates

with said second trait in said second species, said locus is identified as said molecular target, wherein at least one of steps (a), (b), and (c) is performed by a suitably programmed computer.

Claim 178, as amended, specifies a method of identifying a molecular target for a second trait in a second species, the method comprising:

(a) identifying a first gene in a segregating population that is causal for a first trait exhibited by all or a portion of said segregating population, wherein each member of said segregating population is a member of a first species and wherein said second trait in said second species corresponds to said first trait in said first species;

(b) identifying a locus in the genome of the second species that is (1) linked to said second trait and (2) maps to the position in the genome of said first species where said first gene resides; and

(c) determining whether a marker or a haplotype in said corresponding locus in the genome of the second species associates with said second trait, wherein, when said marker or said haplotype associates with said second trait in said second species, said locus is identified as said molecular target, wherein at least one of steps (a), (b), and (c) is performed by a suitably programmed computer.

Claim 188, as amended, specifies a method of identifying a molecular target for a second trait in a second species, the method comprising:

(a) identifying a first gene in a segregating population that is causal for a first trait exhibited by all or a portion of said segregating population, wherein each member of said segregating population is a

member of a first species and wherein said second trait in said second species corresponds to said first trait in said first species; and

(b) identifying a second gene in the genome of the second species that is orthologous to said first gene and in which (i) the variation of the abundance of the second gene across biological samples taken from a plurality of members of said second species and (ii) the variation of the second trait across said plurality of members of said second species are associated, wherein said second gene is identified as said molecular target, and wherein at least one of steps (a) and (b) is performed by a suitably programmed computer.

Claims 168, 178, and 188, as amended, are drawn to statutory subject matter and comply with the utility requirement under 35 U.S.C. § 101 because the identification of a molecular target for a second trait in a second species as performed by the method of Claims 168, 178, and 188 have substantial practical application. In each of Claims 168, 178, and 188, the useful result (the identification of a molecular target for a second trait in a second species) is clearly stated, and the specification provides ample teaching for one skilled in the art to recognize what the result means (and thus how it can be used).

For example, the instant specification states: "The present invention provides an improvement over the art by uniquely combining gene expression approaches with genetic approaches in order to determine the genes associated with traits, such as complex human diseases." (Specification at page 9, lines 26-28.)

The instant Specification further states:

The methods of the present invention are used to identify gene-gene interactions, gene-phenotype interactions, and biological pathways

linked to complex traits in one species (target species, first species) using data from another species (reference species, second species). For example, in one embodiment of the present invention, genes identified using the processing steps described in Section 5.1, above, and illustrated in FIG. 2, are used to identify genes associated with a complex trait in a reference species. Then, the genes that are orthologs of the genes identified in the reference species are identified in the target species. In another example, genes identified using the processing steps described in Section 5.16, above, and illustrated in FIG. 19, are used to identify genes associated with a complex trait in the reference species. Then, the genes that are the orthologs of the genes identified in the reference species are identified in a target species. Orthologs represent the same protein from different species. That is, an ortholog is a gene that is equivalent in two different species by sharing the same common ancestor. Stated differently, an ortholog is a functional counterpart of a gene in another genome that has arisen from speciation. See, for example, Fitch, 1970, *Systematic Zoology* 19:99-113. [Specification at page 117, line 20, to page 118, line 3.]

Additionally, the instant specification states:

In some embodiments, before a putative target cellular constituent is biologically validated in mice, association studies can be carried out in human populations to provide a source of validation in humans. Associating a gene in a human population with a clinical trait, where the gene in mouse 1) was physically co-localized with a cQTL for the

corresponding clinical trait in a segregating mouse population, 2) gave rise to a cis-acting QTL with respect to its transcription, and 3) was significantly genetically interacting with the clinical trait QTL, is itself a very powerful validation of a gene's role in the complex trait of interest. See, also, U.S. Provisional Patent Application 60/436,684 filed Dec. 27, 2002. The combined validation in mouse and human provides all that is necessary to move a target forward in a discovery program. [Specification at page 261, line 20, to page 262, line 3.]

As further described in the instant specification:

The present section provides an example of how the systems and methods of the present invention can be used to associate genes with traits using cross species data. This example builds upon the discovery of the four murine candidate genes identified in Section 6.7.1, above. In Section 6.7.1, four genes were discovered on mouse chromosome number 2 by co-localizing cQTL for the obesity related traits (1) subcutaneous fat pad mass (FIG. 20, curve 2002), (2) perimetrial fat pad mass (FIG. 20, curve 2004), (3) omental fat pad mass (FIG. 20, curve 2006), and (4) adiposity (FIG. 20, curve 2008) with four eQTL with lod scores greater than 3.0 that correspond to genes whose physical locations are within the vicinity (e.g., 2 cM) of the four cQTL. The four mouse genes are (1) RIKEN cDNA 2610042014 (NM\_025575) (FIG. 20, curve 2012-4), (2) ATPase, class It, type 9A (NM-015731) (FIG. 20, curve 2012-3), (3) RIKEN cDNA2610100K07 (NM-025996) (FIG. 20,

curve 2012-2), and (4) zinc finger protein 64 (NM-009564) (FIG. 20, curve 2012-1).

The region of mouse chromosome 2 in which curves 2002 through 2012 are found is homologous to human chromosome region 20q12-q13.12. This region of the human genome has previously been linked to human obesity-related phenotypes. See, for example, Borecki et al., 1994, Obesity Research 2, 213-219 and Lemberas et al., 1997, J. Clin. Investigation 100, 1240-7. The data described in section 6.7.1. strongly suggests that the human genes in human chromosome region 20q12-q13.12 that correspond to the mouse genes are associated with obesity. Therefore, following the methods and systems of the present invention, the human genes that correspond to the four mouse genes identified in Section 6.7.1, above, were characterized. A summary of this characterization is provided in Tables 2 and 3 below. In Table 6, the nucleotide information for the four mouse genes and the four corresponding human genes is provided. In Table 4, the protein products of the four mouse genes and the four corresponding human genes is provided. [Specification at page 297, lines 5-30.]

Thus, the specification provides ample teaching for one of skill in the art to recognize the practical application provided by the identification of a molecular target for a second trait in a second species in the manner specified by Claims 168, 178, and 188.

Claims 169-177, 179-187, and 189-194 depend from Claims 168, 178, and 188, respectively, and are thus patentable under 35 U.S.C. § 101 for at least the same reasons as

Claims 168, 178, and 188. Accordingly, applicants respectfully submit that the 35 U.S.C. § 101 rejection of Claims 168-194 be withdrawn.

The Rejection of Claims 168-194 Under 35 U.S.C. § 112 for Lack of Enablement

Claims 168-194 stand rejected under 35 U.S.C. § 112 for lack of enablement. The Examiner asserts that since the claimed invention is not supported by either a specific, substantial asserted utility, or a well established utility, one skilled in the art would not know how to use the claimed invention. Applicants respectfully traverse this ground of rejection. Contrary to the Examiner's assertion, as described *supra*, the identification of a molecular target for a second trait in a second species as performed by the method of Claims 168, 178, and 188 have substantial practical application. In each of Claims 168, 178, and 188, the useful result (the identification of a molecular target for a second trait in a second species) is clearly stated, and the specification provides ample teaching for one skilled in the art to recognize what the result means, and thus how it can be used. Accordingly, removal of this ground of rejection is respectfully requested.

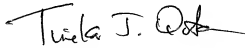


CONCLUSION

Applicants believe that all of the pending claims are in condition for allowance. Reconsideration and favorable action are requested. If any issues remain that may be expeditiously addressed in a telephone interview, the Examiner is encouraged to telephone applicants' attorney at 206.695.1655.

Respectfully submitted,

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A handwritten signature in black ink, appearing to read "Tineka J. Quinton", with a stylized flourish at the end.

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